Claims

1) A method for the analysis of cytosine methylation, characterized in that:

a) the DNA to be investigated is chemically or enzymatically converted so that 5-methylcytosine remains unchanged, while unmethylated cytosine is converted to uracil or to another base which differs from cytosine in its base pairing behavior,

b) the converted DNA is hybridized to oligonucleotides, whereby the DNA of one methylation status forms hybrids with erroneous base pairings, while the DNA of the other methylation status forms hybrids without erroneous base pairings or does not form hybrids,

c) one strand of the erroneously paired hybrids is enzymatically cleaved,

d) the uncleaved DNA or the cleaved fragments are detected,

e) the methylation status of the investigated DNA is concluded from the detection signal generated in step d).

2) The method according to claim 1, further characterized in that in step b), the DNA of one methylation status forms hybrids with erroneous base pairings, while the DNA of the other methylation status forms hybrids without erroneous base pairings.

3) The method according to claim 1, further characterized in that in step b), the DNA of one methylation status forms hybrids with erroneous base pairings, while the DNA of the other methylation status does not form hybrids.

4) A method for the analysis of cytosine methylation, characterized in that:

a) the DNA to be investigated is chemically or enzymatically converted so that 5-methylcytosine remains unchanged, while unmethylated cytosine is converted to uracil or to another base which differs from cytosine in its base pairing behavior,

b) the converted DNA is hybridized to oligonucleotides, whereby the DNA to be detected forms hybrids with erroneous base pairings,

c) the oligonucleotide strand of the erroneously paired hybrids is enzymatically cleaved,

d) the cleaved oligonucleotide fragments are detected,

e) the methylation status of the investigated DNA is concluded from the detection signal generated in step d).

5) A method for the analysis of cytosine methylations, characterized in that:

a) the DNA to be investigated is chemically or enzymatically converted so that 5-methylcytosine remains unchanged, while unmethylated cytosine is converted to uracil or to another base which differs from cytosine in its base pairing behavior,

b) the converted DNA is hybridized to oligonucleotides, whereby the background DNA forms hybrids with erroneous base pairings,

c) the DNA strand of the erroneously paired hybrids is enzymatically cleaved,

d) the uncleaved DNA is detected,

e) the methylation status of the investigated DNA is concluded from the detection signal generated in step d).

6) The method according to claim 5, further characterized in that the background DNA forms several erroneous base pairings with the oligonucleotides.

7) The method according to at least one of claims 5 or 6, further characterized in that the oligonucleotides utilized in step b) are simultaneously utilized as primers or probes in a later amplification step.

8) The method according to at least one of claims 1-3 or 5-7, further characterized in that the detection in step d) is carried out by means comprising a nucleic acid amplification.

9) The method according to claim 8, further characterized in that the amplification or the detection of the amplificates is carried out in a methylation-specific manner.

10) The method according to one of claims 8 or 9, further characterized in that several fragments are simultaneously amplified.

11) The method according to at least one of claims 1-3 or 5-10, further characterized in that the detection in step d) is made by means of a microarray.

12) The method according to at least one of claims 1-11, further characterized in that in step c) a DNA repair enzyme is utilized.

13) The method according to claim 12, further characterized in that said DNA repair enzyme is selected from the group consisting of Mut Y, Mug protein, DNA glycosylase and TDG enzyme.

14) The method according to claims 12 and 13, further characterized in that heat-stable enzymes are utilized.

15) The method according to claim 13, further characterized in that a heat-stable TDG enzyme is utilized.

16) The method according to at least one of claims 1-15, further characterized in that steps c) to e) are conducted simultaneously.

17) The method according to claims 1-16 for the diagnosis or prognosis of cancer disorders or other diseases associated with a change in the cytosine methylation status, for predicting undesired drug interactions, for establishing a specific drug therapy, for monitoring the success of a drug therapy, for distinguishing cell types or tissues and for investigating cell differentiation.

18) The method according to claims 1-16 for the early diagnosis of cancer disorders or other diseases associated with a change in the cytosine methylation status.

19) The method according to claim 1 to 18 wherein the DNA to be investigated has been isolated from a body fluid sample of an individual.

20) The method according to claim 1 to 18 wherein the DNA to be investigated has been isolated from a serum, plasma, sperm, urine or stool sample of an individual.

21) A kit, comprising at least one oligonucleotide probe and a repair enzyme as well as optionally, a polymerase and additional reagents necessary for a PCR.

22) A kit, comprising a repair enzyme and at least one oligonucleotide probe, characterized as hybridizing to nucleic acids, which have been converted according to step a in claim 1, and wherein said hybridization comprises at least one mismatching base position.

23) A kit, comprising a repair enzyme; at least one oligonucleotide probe, characterized as hybridizing to nucleic acids, which have been converted according to step a in claim 1, wherein said hybridization comprises at least one mismatching base position; a polymerase and additional reagents necessary for a PCR.